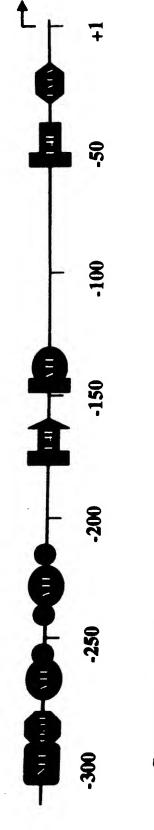


FIGURE 1



Symbol Legend:

- NF-I binding site centered around -300
 - Oct1 binding site positioned near -285
- ATF binding sites near -260, -230, and -140

Sp1 binding sites near -255, -240, and -220

- E4F inverted repeat binding sites near -165 and -50
- EivF binding sites near -165 and -50

 E4TF1 binding site positioned around -140

 TATA box positioned near -30

 transcriptional start site denoted as +1

FIGURE 2

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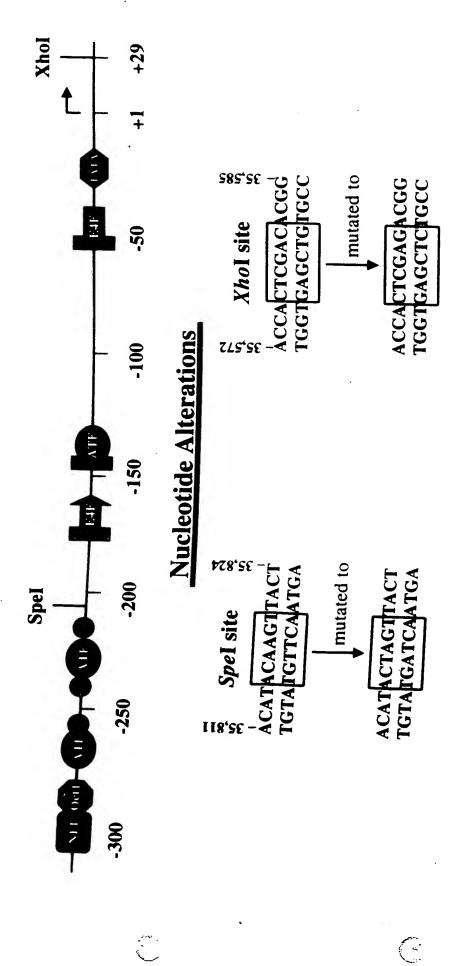
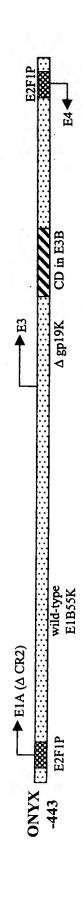


FIGURE 3

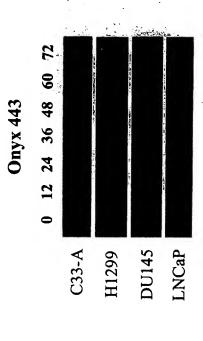
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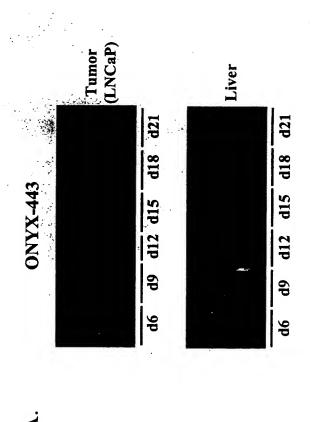


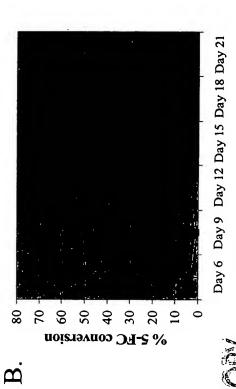
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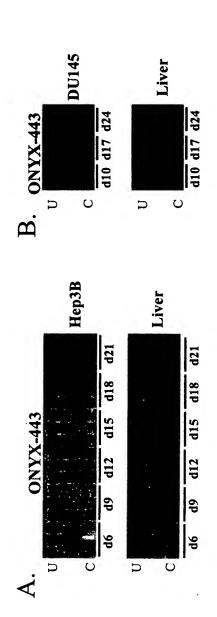
Hepatocytes

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Figure 1. Genomic changes in ONYX-4XX. ITR: inverted terminal repeat; ψ: Viral packaging sequence; E2F1P: E2F1 promoter; H: Hind III site; B: BamH I site; X: Xho I site; S: Spe I

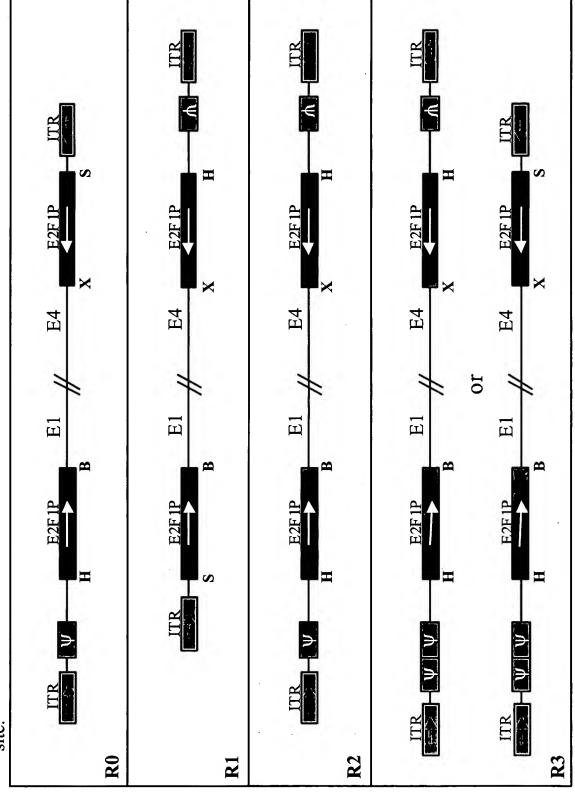
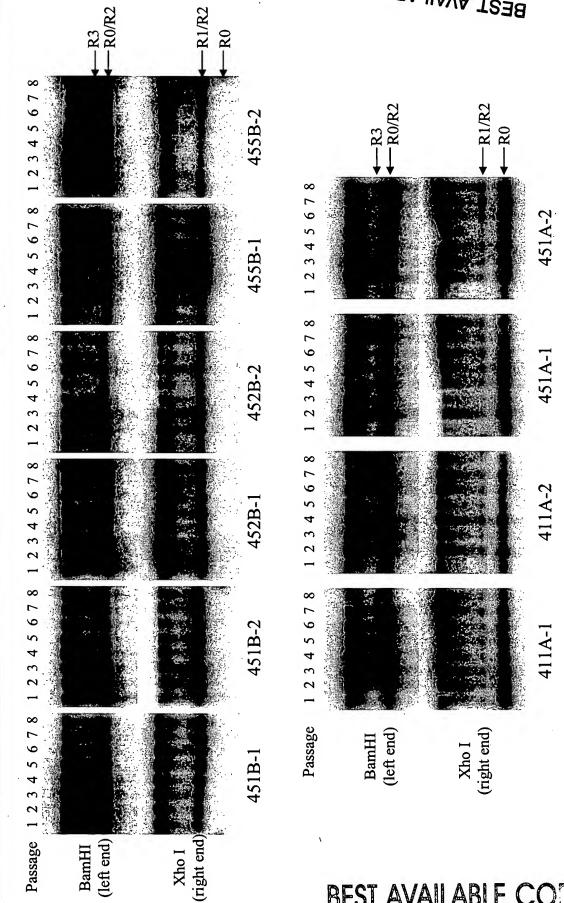


Figure 8. Sequencing Confirmation of ONYX-4XX R2 Termini

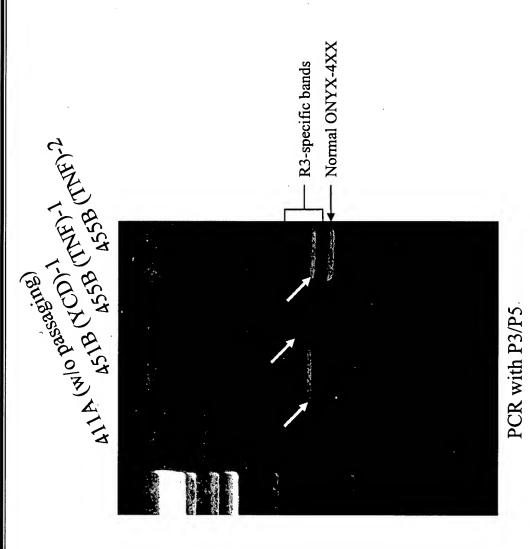
	CATCATCAATAATATATCCFTAITFINGGATIGAAGCCAATATGATAATGAGGGGTGGAGTTTGTGAGGGGGGGG	90 100 110 120 130 140 150 160 160 160 160 160 160 160 160 160 16	170 180 190 200 210 220 230 240 ingcraaaagigaccaargiracacagaagigacaarirircacagaagigacaarirircacagaagiririragaagigacaargiracaagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaarirircacagaagigacaaarirircacagaagigacaaarirircacagaagigacaaagigacaaarirircacagaagigacaaagigacaaagigacaaaagigacaaagigacaaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaaagigacaaaagigacaaaagigacaaaagigacaaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaaagigacaaaagigacaaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaagigacaaaagigacaaaagigacaaaagigacaaaagigacaaaagigacaaaagigaaagigaaaagigaaaagigaaagigaaaagigaaaaagigaaaagigaaagigaaagigaaagigaaaagigaaaagigaaaagigaaaagigaaaagigaaaagigaaaaagigaaaagigaaaagigaaaagigaaagigaaagigaaagigaaagigaaaagigaaaagigaaagigaaagigaaagigaaagigaaaagigaaaaagigaaagigaaagigaaaaaa	TRAATITIGGGCGTAACCGAGTAAGATITIGGCCATITITICGCGGGAAAACTGAATAAGAGGAAGTGAAATCTGAATAATITIT TRAATITIGGGCGTAACCGAGTAAGATITIGGCCATITITICGCGGGAAAACTGAATAAGAGGAAGTGAAATCTGAATAATITIT TAAATTIGGGCGTAACCGAGTAAGATTIGGCCATITITICGCGGGAAAAACTGAATAAGAGGAAGTGAAATCTGAATAATITIT ONYX-4XX-R2 left end	330 340 350 360 370 380 390 400 GIGITACICATAGCCCCCCCCCCCCCCCCCCCCCCCCCCC
80	o wild onxx-	160 ire wild ire onyx-	240 	320 TT Wild TT ONYX-	400 TTT Wild
~	555555 5555555 5555555 555555 55555 5555	ACGGAT	2 GITGIP	STAATTT	4 FIGITITE
7,0	ACCTGCC CACCTGCC	150 ATGTAAGCC ATGTAAGCC	230 IAGGCGGA IAGGCGGA IAGGCGGAI	310 AAATCTGA/ AAATCTGA/ AAATCTGA/	330 340 350 360 370 380 390 400 GROTTACTCATAGCGCGTAATATTTGTCTAGGGCGCGTTTTACGTGGAGACTTCGCCCAGGTGTTTTT Wild type ad5 left en
09	SCAGITICI SCAGITICI SCAGITICI	140 GGGAACAC GCGGAACAC GCGGAACAC	220 GOCGGTITI GCGCGGTITI SCGCGGTITI	300 GAGGAAGTG GAGGAAGTG GAGGAAGTG	380 GTGGAGAC GAAGCTTCG
50	ATGAGGGGTIV ATGAGGGGGT	130 IGCAAGTOTO IGCAAGTOTO IGCAAGTOTO	210 aacaaritiro aacaaritiro aacaaritiro	290 AACTGAATAA AACTGAATAA AACTGAATAA	370 IGACCGITITA
40	PATATGATA PATATGATA	120 AGTGTGATGT AGTGTGATGT	200 DACAGGAAGIN DACAGGAAGIN	280 FTCGCGGGAA FTCGCGGGAA FTCGCGGGAA	360 SCGGGGACTT
30	SATTGAAGCC SCATTGAAGCC SCATTGAAGCC	110 STGTGGGGAV STGTGGGGAV	190 GCCGGTGTAC GCCGGTGTAC	270 FINGGCCATT FINGGCCATT	350 STCTAGGGCC STCTAGGGCCC
20	'ATCATCAATAATATACCTTATTTTG 'ATCATCAATAATATACCTTATTTTG	100 RACGIAGIA RACGIAGIA RACGIAGIA	180 iritigenene iritigenene	250 260 IPAATITIGGGCGTAACCGAGTAAGAI IPAATITIGGGCGTAACCGAGTAAGAI IPAATITIGGGCGTAACCGAGTAAGAI	340 GIRATATITIC GIRAITATITIC
10	CAATAATATI CAATAATATI CAATAATATI	90 CGGGGGGGG CGGGGCGGG	170 AAGTGACGTT AAGTGACGTT	250 TGGGCGTAAC TGGGCGTAAC	330 CTCATAGCGC CTCATAGCGC
	CATCAN CATCAN	TGGGAA TGGGAA TGGGAA			
		81 65 65	161 145 145	241 225 225	321

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Figure 9 Southern Analysis of Viruses from Serial Passaging



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Figure 11. Duplication of Packaging Sequence

	GACCITITICGICCOCCCGIGIACACACACACACACACACACACACACACACACA	GIIGIAGIAAAITIGGG 107 bp YCD1.SEQ IGIIGIAGIAAAITIGGG 115 bp INF2.SEQ GAIGIIGIAGIAAAITIGGG 202 bp INF1.SEQ KAIGIIGIA <u>GIAAAAAAA</u> GG Ad5 packaging seq
18 19 81 62	GGIBACCCEGIBACENTITIGGCCENTITICGGGGERAAACHCEAAIBACHCHCAAIBATTTTGIGTTACTCA 107 bp YCD1.SEQ GGIBACCCEGIBACENTITIGGCCENTITICGGGGERAACHCEAAIGTGAATCHCEAAIBATTTTGIGTTACTCA 115 bp TNF2.SEQ GGIBACCCEGIBACENTITIGGCCENTITICGGGGERAACHCEAAIBAGGGAAGHCEAAIBATTTTGIGTTACTCA 202 bp TNF1.SEQ CGIBACCCEGIBACENTITICGGGGERAAACHCEAAIBACEGAAGHCEAAIGTGEAAITTTGIGTTACTCA Ad5 packaging seq AII AII	ATTITICICITACICA 107 bp YCD1.SEQ ATTITICICITACICA 115 bp TNF2.SEQ ATTITICICITACICA 202 bp TNF1.SEQ AMMUNICICITACICA Ad5 packaging seq AIV
98 99 161 142	98 TRACCOCTRATATITICT 161 TRACCOCTRATATITICTCTRACCOCCCCCCCCCCCCTTTTCACCCTT 142 TRACCOCTRATATITICTCTRACCOCCCCCCCCCCCCCCCCCTTTTCACCCTTTCACCAC	107 bp YCD1.SEQ 115 bp TNF2.SEQ 202 bp TNF1.SEQ Ad5 packaging seq

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